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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/817,318	03/26/2001	Susana Salceda	DEX-0199	1254

26259 7590 07/05/2002

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EXAMINER
DAVIS, MINH TAM B

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 07/05/2002 9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/817,318	SALCEDA ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears n the cover sh et with the correspond nc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *7,8,10-22,24 and 25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,9 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's election with traverse of group I, claims 1-6, 9, 23, SEQ ID NO:1 in Paper No. 9 is acknowledged. The traversal is on the ground(s) that 1) a search for the MSG polynucleotides would also reveal art relating to polypeptides encoded by thereby, thus it does not appear to be a serious burden for the Examiner to search and examine groups III-VII, 2) No evidence is shown to support the contention that the groups have acquired separate status in the art, since the numbers of class and subclass have been left blank, 3) There are no claims reciting limitations for only one polynucleotide or polypeptide encoded thereby and not for another, thus according to MPEP 806.04(f), restriction to one of the polynucleotide of SEQ ID Nos: 1-20 is improper as the polynucleotides are related species and 4) The claims are not drawn to a large number of species, only 20 sequences are set forth, and thus it would not be a serious burden for the Examiner to search all the sequences together.

This is not found persuasive because of the following reasons: 1) A MSG polynucleotide is structurally distinct from its encoded polypeptide, and the searches for a MSG polynucleotide and its encoded protein are not co-extensive and it would be a burden for the Examiner to search them together, 2) Although the numbers of class and subclass were inadvertently left blank, after review and reconsideration, it is clear that different groups are patentably distinct for reasons set forth in previous Office action, 3) Claim 1 is an improper implied Markush claim, since it is clearly meant to encompass different polynucleotides having different structure. Further, MPEP 2173.05(h) provides that when the Markush group occurs in a claim reciting a process or a combination it is

sufficient if the members of the group are disclosed in the specification to possess at least one property in common which is responsible for their function in the claimed relationship and it is clear from their very nature or from the prior art that all of them possess this property. The members of the implied Markush groups recited in claim 1 do not share a common property, nor do they function by a common mechanism. Thus it is proper to restrict SEQ ID Nos: 1-20 into different groups and not species , and 4) The searches for SEQ ID Nos: 1-20 are not co-extensive, and it would be a burden for the Examiner to search them together.

The requirement is still deemed proper and is therefore made FINAL.

Accordingly, claims 1-6, 9, 23 are examined in the instant application, wherein claims 1-6, 9, 23 are examined only to the extent of SEQ ID NO:1 or Mam021.

OBJECTION

Claim 1 is objected to because claim 1 recites non-elected sequences of SEQ ID Nos: 2-20.

Claim Rejections - 35 USC § 112, SECOND PARAGRAPH

Claims 1-6, 9 and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claims 1-6, 9 are indefinite for the use of the language " hybridizes under stringent conditions" in claim 1, and "hybridizes" in claim 2. The "stringent conditions" in

claim 1 and the hybridization conditions in claim 2 are not defined by the claims (which read on the full range of hybridization conditions or the full range of stringent conditions), the specification does not provide a standard for ascertaining the requisite degree of hybridization conditions or stringent conditions and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention and would not be able to determine the metes and bounds of the claims.

2. Claims 5, 6, 9 and 23 are indefinite for the use of the abbreviated language "MSG" polypeptide. This rejection could be obviated by amending the claims, for example, to recite the full name of MSG.

3. Claims 5, 6 23 are indefinite for the use of the language " a MSG polypeptide". It is not clear which of the MSG polypeptides encoded by SEQ ID NO:1-20 is referred to.

Claim Rejections - 35 USC § 112 FIRST PARGRAPH, WRITTEN DESCRIPTION

The instant specification does not contain a written description of the invention in such full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing.

The claims 1-6, 9 are drawn to 1) a nucleic acid sequence which "hybridizes under stringent conditions" to an antisense sequence of SEQ ID NO:1, 2) a polynucleotide "comprising a fragment" of SEQ ID NO:1, and 3) an antisense oligonucleotide which "hybridizes" to SEQ ID NO:1.

The claims are further drawn to vectors comprising the above nucleic acid sequence, host cells transfected with said sequence, a method for expressing said nucleic acid sequence, and a method for producing a cell expressing said a MSG polypepeptide.

It is noted that "hybridizes under stringent conditions" encompasses different stringent conditions, from very low to high stringency conditions and that "hybridizes" encompasses different hybridization conditions, including very low stringency. Thus the claims encompass unrelated sequences that are attached to SEQ ID NO:1 or to an antisense of SEQ ID NO:1.

It is also noted that a polynucleotide "comprising a fragment" of SEQ ID NO:1 encompasses unrelated polynucleotide sequences which only share with SEQ ID NO:1 15 nucleotides.

The specification discloses an isolated cDNA sequence, SEQ ID NO: 1.

The instant disclosure of a single species of nucleic acid does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera including full-length genes. A description of a genus of cDNAs may be acheived by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural freatures common to members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The instant specification fails to provide sufficient descriptive information, such as definitive strutural or functional

features of the claimed genus of polynucleotides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no description, however, of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural freatures that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides encompassed and no identifying characteristic or property of the instant polynucleotides is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed.

Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of specific nucleotide sequences and the ability to screen, is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed. Thus, only an isolated polynucleotide comprising SEQ ID NO: 1, but not the full breadth of the claims meet the written description provisions of 35 USC 112, first paragraph.

Claim Rejections - 35 USC § 112 FIRST PARGRAPH, ENABLEMENT

Claim 23 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one

skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 23 is drawn to a vaccine comprising a vector expressing a MSG polypeptide which induces an immune response against the MSG polypeptide in a mammal.

Due to the indefinite language of claim 23 it is assumed for the purpose of compact prosecution that MSG polypeptide is a polypeptide encoded by a mammary gland cancer specific gene of SEQ ID NO:1.

Claim 23 encompass a vector expressing a MSG polypeptide which induces an immune response against the MSG polypeptide in a mammal for use in treating mammary gland cancer.

The specification discloses detection of a mammary gland specific polynucleotide of SEQ ID NO:1, or Mam021, which is overexpressed in mammary gland cancer as compared to normal tissues (table 2 on pages 57-59, and page 60). The specification contemplates treatment of mammary gland cancer comprising administering antibodies specific for MSG polypeptide, or administering a vaccine comprising a vector which directs expression of MSG polypeptide *in vivo* to induce immunological response and to produce antibodies in vivo (p.43-44).

One cannot extrapolate the teaching of the specification to the enablement of the claims for the following reasons: 1) It is unpredictable that inhibiting the expression of a MSG polypeptide encoded by SEQ ID NO:1 by an antibody produced by a MSG polypeptide encoded by SEQ ID NO:1 would be useful for treating cancer, because it is

questionable that SEQ ID NO:1 is responsible for mammary gland cancer, and because it is questionable that SEQ ID NO:1 actually is translated into a protein in vivo, and 2) it is well known in the art that cancer therapy treatment is unpredictable.

Although SEQ ID NO:1 is found to be overexpressed in mammary gland cancer, one cannot extrapolate that SEQ ID NO:1 is responsible for mammary gland cancer, because it is not known whether development of mammary gland cancer is caused by the overexpression of SEQ ID NO:1, or whether overexpression of SEQ ID NO:1 is the end product of mammary gland cancer. Thus it is unpredictable that an antibody produced by the MSG polypeptide expressed by a vector comprising SEQ ID NO:1 *in vivo* would be effective in treating mammary gland cancer.

Further, although SEQ ID NO:1 is overexpressed in mammary gland cancer, it is unpredictable that SEQ ID NO:1 is translated into protein, and if translated, is overexpressed in mammary gland cancer. It is well known in the art that regulation of mRNA translation is one of the major regulatory steps in the control of gene expression (Jansen, M et al, 1995, Pediatric Res, 37 (6): 681-686). Further, those of skill in the art recognize that expression of mRNA, specific for a tissue type, does not dictate nor predict the translation of such mRNA into a polypeptide. For example, Alberts et al. (Molecular Biology of the Cell, 3rd edition, 1994, page 465) teach that translation of ferritin mRNA into ferritin polypeptide is blocked during periods of iron starvation. Likewise, if excess iron is available, the transferrin receptor mRNA is degraded and no transferrin receptor polypeptide is translated. Many other proteins are regulated at the translational level rather than the transcriptional level. For instance, Shantz and Pegg

(Int J of Biochem and Cell Biol., 1999, Vol. 31, pp. 107-122) teach that ornithine decarboxylase is highly regulated in the cell at the level of translation and that translation of ornithine decarboxylase mRNA is dependent on the secondary structure of the mRNA and the availability of eIF-4E, which mediates translation initiation. McClean and Hill (Eur J of Cancer, 1993, vol. 29A, pp. 2243-2248) teach that p-glycoprotein can be overexpressed in CHO cells following exposure to radiation, without any concomitant overexpression of the p-glycoprotein mRNA. In addition, Fu et al (EMBO Journal, 1996, Vol. 15, pp. 4392-4401) teach that levels of p53 protein expression do not correlate with levels of p53 mRNA levels in blast cells taken from patients with acute myelogenous leukemia, said patients being without mutations in the p53 gene. Yokota, J et al (Oncogene, 1988,Vol.3, pp. 471-475) teach that the retinoblasma (RB) 115 kD protein is not detected in all nine cases of lung small-cell carcinoma, with either normal or abnormal size mRNA, whereas the RB protein is detected in three of four adenocarcinomas and all three squamous cell carcinomas and one of two large cell carcinomas expressing normal size RB mRNA. Thus, predictability of protein translation or the extent of translation is not solely contingent on mRNA expression due to the multitude of homeostatic factors affecting transcription and translation. For the above reasons, one of skill in the art would not be able to predict if SEQ ID NO:6 is translated into a polypeptide expression product, or even if translated, whether it is overexpressed.

Moreover, the specification provides no exemplification of or guidance on how to use the claimed vaccine formulation or antigen for active immunotherapy in humans.

The goal of tumor vaccination is the induction of tumor immunity to prevent tumor recurrence and to eliminate residual disease. However, Ezzell (J. NIH Res, 1995, 7:46-49) reviews the current thinking in cancer vaccines and states that tumor immunologists are reluctant to place bets on which cancer vaccine approach will prove effective in the long run (see the entire document, particularly last paragraph) and further states that no one is very optimistic that a single peptide will trigger an immune response strong enough to eradicate tumors or even to prevent the later growth of micrometastases among patients whose tumors have been surgically removed or killed by radiation or chemotherapy (p 48, para 6). In addition, Spitler (Cancer Biotherapy, 1995, 10:1-3) recognizes the lack of predictability of the nature of the art when she states that "Ask practicing oncologists what they think about cancer vaccines and you're likely to get the following response: "cancer vaccines don't work". Ask a venture capitalist or the director of product development at a large pharmaceutical company and you're likely to get the same response." (p 1, para 1). Furthermore, Boon (Adv Can Res, 1992, 58:177-210) teaches that for active immunization in human patients we have to stimulate immune defenses of organisms that have often carried a large tumor burden. Establishment of immune tolerance may therefore have occurred and it may prevent immunization and several lines of evidence suggest that large tumor burdens can tolerize or at least depress the capability to respond against the tumor (p. 206, para 2). In addition, Boon teaches even if activated CTLs are significantly increased, the therapeutic success remains unpredictable due to inconsistencies in antigen expression or presentation by tumor cells (p.178, paragraph before last paragraph).

Moreover, as written the claims encompass gene therapy. The state of the art at the time of filing was that the combination of vector, promoter, protein, cell, target tissue, level of expression and route of administration required to target the tissue of interest and obtain a therapeutic effect using gene therapy was unpredictable. For example, Miller (1995, FASEB J., Vol. 9, pages 190-199) review the types of vectors available for *in vivo* gene therapy, and conclude that "for the long-term success as well as the widespread applicability of human gene therapy, there will have to be advances...targeting strategies outlined in this review, which are currently only at the experimental level, will have to be translated into components of safe and highly efficient delivery systems" (page 198, column 1). Deonarain (1998, Expert Opin. Ther. Pat., Vol. 8, pages 53-69) indicate that one of the biggest problems hampering successful gene therapy is the "ability to target a gene to a significant population of cells and express it at adequate levels for a long enough period of time" (page 53, first paragraph). Deonarain reviews new techniques under experimentation in the art which show promise but states that such techniques are even less efficient than viral gene delivery (see page 65, first paragraph under Conclusion section). Verma (Sept. 1997, Nature, Vol. 389, pages 239-242) reviews vectors known in the art for use in gene therapy and discusses problems associated with each type of vector. The teachings of Verma indicate a resolution to vector targeting has not been achieved in the art (see entire article). Verma also teaches appropriate regulatory elements may improve expression, but it is unpredictable what tissues such regulatory elements target (page 240, sentence bridging columns 2 and 3). Crystal (1995, Science, Vol. 270, page 404-

410) also reviews various vectors known in the art and indicates that "among the design hurdles for all vectors are the need to increase the efficiency of gene transfer, to increase target specificity and to enable the transferred gene to be regulated" (page 409).

In view of the above, one of skill in the art would be forced into undue experimentation to practice the claimed invention.

Claim Rejections - 35 USC § 112, FIRST PARAGRAPH, SCOPE

1. If Applicant could overcome the above 112, first paragraph rejection, claims 1-6, 9 are still rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO:1, does not reasonably provide enablement for a nucleic acid sequence which "encodes" the same protein as that encoded by SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claims 1-6, 9 are drawn to a nucleic acid sequence which "encodes" the same protein as that encoded by SEQ ID NO:1.

Claims 1-6, 9 encompass a nucleic acid sequence which is translated in tissue into the same protein as that encoded by SEQ ID NO:1.

One of skill in the art would not be able to predict if SEQ ID NO:1, or its degenerate variant, is translated into a polypeptide expression product, or even if translated, whether it is overexpressed. It is well known in the art that regulation of

mRNA translation is one of the major regulatory steps in the control of gene expression (Jansen, M et al, 1995, Pediatric Res, 37 (6): 681-686). Further, those of skill in the art recognize that expression of mRNA, specific for a tissue type, does not dictate nor predict the translation of such mRNA into a polypeptide. For example, Alberts et al. (Molecular Biology of the Cell, 3rd edition, 1994, page 465) teach that translation of ferritin mRNA into ferritin polypeptide is blocked during periods of iron starvation. Likewise, if excess iron is available, the transferrin receptor mRNA is degraded and no transferrin receptor polypeptide is translated. Many other proteins are regulated at the translational level rather than the transcriptional level. For instance, Shantz and Pegg (Int J of Biochem and Cell Biol., 1999, Vol. 31, pp. 107-122) teach that ornithine decarboxylase is highly regulated in the cell at the level of translation and that translation of ornithine decarboxylase mRNA is dependent on the secondary structure of the mRNA and the availability of eIF-4E, which mediates translation initiation. McClean and Hill (Eur J of Cancer, 1993, vol. 29A, pp. 2243-2248) teach that p-glycoprotein can be overexpressed in CHO cells following exposure to radiation, without any concomitant overexpression of the p-glycoprotein mRNA. In addition, Fu et al (EMBO Journal, 1996, Vol. 15, pp. 4392-4401) teach that levels of p53 protein expression do not correlate with levels of p53 mRNA levels in blast cells taken from patients with acute myelogenous leukemia, said patients being without mutations in the p53 gene. Yokota, J et al (Oncogene, 1988,Vol.3, pp. 471-475) teach that the retinoblasma (RB) 115 kD protein is not detected in all nine cases of lung small-cell carcinoma, with either normal or abnormal size mRNA, whereas the RB protein is

detected in three of four adenocarcinomas and all three squamous cell carcinomas and one of two large cell carcinomas expressing normal size RB mRNA. Thus, predictability of protein translation or the extent of translation is not solely contingent on mRNA expression due to the multitude of homeostatic factors affecting transcription and translation. For the above reasons, one of skill in the art would not be able to predict if SEQ ID NO:1 or its degenerate variant is translated into a polypeptide expression product, or even if translated, whether it is overexpressed. In view of the above, one of skill in he art would be forced into undue experimentation to practice the claimed invention.

2. If Applicant could overcome the above 112, first paragraph rejection, claims 1-6, 9 are still rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO:1, does not reasonably provide enablement for a nucleic acid sequence which "hybridizes under stringent conditions" to an antisense of SEQ ID NO:1, a polynucleotide "comprising a fragment" of SEQ ID NO:1, and an antisense oligonucleotide which "hybridizes" to SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims 1-6, 9 are drawn to 1) a nucleic acid sequence which "hybridizes under stringent conditions" to an antisense sequence of SEQ ID NO:1, 2) a polynucleotide "comprising a fragment" of SEQ ID NO:1, and 3) an antisense oligonucleotide which "hybridizes" to SEQ ID NO:1.

The claims are further drawn to vectors comprising the above sequences and host cells transfected with them.

It is noted that "hybridizes under stringent conditions" encompasses different stringent conditions, from very low to high stringency conditions and that "hybridizes" encompasses different hybridization conditions, including very low stringency. It is well known that the lower the stringency condition the more dissimilar the hybridizing molecule will be from the molecule to which it hybridizes. Thus the claims encompass unrelated sequences that are attached to SEQ ID NO:1 or to an antisense of SEQ ID NO:1.

It is also noted that a polynucleotide "comprising a fragment" of SEQ ID NO:1 encompasses unrelated polynucleotide sequences which only share with SEQ ID NO:1 15 nucleotides.

When given the broadest reasonable interpretation, the claims are clearly intended to encompass a variety of species including full-length cDNAs, genes and protein coding regions. Clearly, it would be expected that a substantial number of the hybridizing molecules encompassed by the claims **would not** share either structural or functional properties with SEQ ID NO:1. For the above reasons, undue experimentation would be required to practice the claimed invention.

3. If Applicant could overcome the above 112, first paragraph rejection, claims 5, 6 are still rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for producing a MSG polypeptide recombinantly encoded by SEQ ID NO:1, or a cell expressing a MSG polypeptide recombinantly encoded by

SEQ ID NO:1, does not reasonably provide enablement for a method for producing "any" MSG polypeptide or a cell expressing "any" MSG polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claims 5, 6 are drawn to a method for producing "a" MSG polypeptide or a cell expressing "a" MSG polypeptide.

Claims 5, 6 encompass a method for producing "any" MSG polypeptide or a cell expressing "any" MSG polypeptide.

It is not clear how any MSG polypeptide could be produced by expressing SEQ ID NO:1, because their structure is completely different, e.g. MSG polypeptides recombinantly encoded by SEQ ID Nos: 2-20, the structure of which are different from SEQ ID NO:1. One of skill in the art would have expected that not any MSG polypeptide would be produced by expressing SEQ ID NO:1.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 9 are rejected under 35 U.S.C. 102(b) as being anticipated by US PN=5837468.

The claims 1-2 are drawn to 1) a nucleic acid sequence which "hybridizes under stringent conditions" to an antisense sequence of SEQ ID NO:1, 2) a polynucleotide comprising a fragment of at least 15 contiguous nucleobases of SEQ ID NO:1, and 2) an antisense oligonucleotide which "hybridizes" to SEQ ID NO:1. Claim 9 is drawn to a MSG for diagnosing mammary gland cancer, comprising a nucleic acid sequence which "hybridizes under stringent conditions" to an antisense sequence of SEQ ID NO:1.

Due to the indefinite language of claim 9, it is assumed for the purpose of compact prosecution that claim 9 reads on a mammary gland cancer specific gene.

. Further, claim 9 recites a MSG for diagnosing mammary gland cancer. However, this limitation is viewed as a recitation of intended use and therefore is not given patentable weight in comparing the claim with the prior art. Claim 9 reads on the ingredient *per se*, which is a nucleic acid sequence which "hybridizes under stringent conditions" to an antisense sequence of SEQ ID NO:1.

PN=5837468 teaches a sequence which is 100% similar to SEQ ID NO:1, from nucleotide 764 to 780, under MPSRCH sequence similarity search (MPSRCH search report, us-09-817-318-1.oli.rni, pages 4-5).

Given the polynucleotide sequence taught by PN=5837468, one of ordinary skill in the art would immediately envision the claimed nucleic acid sequence or oligonucleotide.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 3-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over PN=5,837,468 in view of of US Patent No. 4,889,806 and Sambrook et al, 1989 (Molecular Cloning, A Laboratory Manual, 2nd Edition, Cold Spring Harbor Press, Cold Spring Harbor, p. 16.3-16.4)

The claims 3-6 are drawn to an expression vector containing a nucleic acid sequence which "hybridizes under stringent conditions" to an antisense sequence of SEQ ID NO:1, a host cell containing the vector and a method for producing a MSG polypeptide and a method for producing a host cell expressing a MSG polypeptide.

PN= 5,837,468 disclose as set forth above but differ from the instant invention in that it does not disclose an expression vector containing a nucleic acid sequence which "hybridizes under stringent conditions" to an antisense sequence of SEQ ID NO:1, a host cell containing the vector or a method for producing a MSG polypeptide and a method for producing a host cell expressing a MSG polypeptide.

US Patent No. 4,889,806 teach that with the advent of recombinant DNA and molecular cloning technology it is now conventional to transfer genetic information into plasmids or vectors constructed in vitro and then transferred into host cells and clonally propagated (col 1, lines 18-24).

Sambrook et al teach that cloned genes are conventionally expressed using expression vectors and that expression of cloned proteins have been used to: (1) confirm the identity of a cloned gene by using immunological or functional assays to detect the encoded protein; (2) produce large amounts of proteins of biological interest that are normally available in only limited quantities from natural sources; (3) to study the biosynthesis and intracellular transport of proteins following their expression in various cell types; and (4) to elucidate structure-function relationships by analyzing the properties of normal and mutant proteins (para bridging pages 16.3 and 16.4).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the polynucleotide of PN=5,837,468 with the methods of Sambrook et al and US Patent No. 4,889,806 because US Patent No. 4,889,806 specifically teaches that it is conventional to transfer genetic materials into plasmids or vectors and then transfer the plasmids or vectors into host cells and clonally propagate the genetic material and because Sambrook et al teach that cloned genes are conventionally expressed using expression vectors. One of ordinary skill in the art at the time the invention was made would have been motivated to combine the polynucleotide of PN=5,837,468 with the methods of Sambrook et al and US Patent No. 4,889,806 because Sambrook et al specifically teach that expressed cloned proteins are used to: (1) confirm the identity of a cloned gene by using immunological or functional assays to detect the encoded protein; (2) produce large amounts of proteins of biological interest that are normally available in only limited quantities from natural sources; (3) to study the biosynthesis and intracellular transport of proteins following

their expression in various cell types; and (4) to elucidate structure-function relationships by analyzing the properties of normal and mutant proteins. One of ordinary skill in the art would have been motivated to clone the claimed sequence in a vector, to transfect into a host cells, and to express it with a reasonable expectation of success. One of ordinary skill in the art would have been motivated to clone the claimed sequence in a vector, to transfect into a host cells, and to express it to produce a large quantity of protein of biological interest, as taught by Sambrook et al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 703-305-2008. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANTHONY CAPUTA can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.

MINH TAM DAVIS

May 24, 2002

SUSAN UNGAR, PH.D
PRIMARY EXAMINER